

# Use of losartan in reducing microalbuminuria in normotensive patients with type-2 diabetes mellitus

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## ABSTRACT

Type-2 diabetes mellitus (T2DM) is a global disease and its resultant complication, diabetic nephropathy, is a leading cause of chronic renal failure. Microalbuminuria is an early indicator of diabetic nephropathy and is also an independent risk factor for cardiovascular morbidity. Data have shown that anti-hypertensives like Angiotensin receptor blockers (ARB), and Angiotensin converting enzyme inhibitors (ACEI) reduce microalbuminuria and retards the progression of renal disease effectively in hypertensive T2DM patients. But the effects of ARBs on preventing microalbuminuria and ensuing nephropathy in normotensive patients with T2DM is yet to be fully established. To assess the anti-microalbuminuric effects of losartan therapy in normotensive T2DM patients. Interventional Phase Two Clinical Trial was done. Study was done at Diabetic Clinic, Jinnah Hospital Lahore, Pakistan over 8 months. A total of 171 normotensive patients with T2DM and microalbuminuria. After informed consent and baseline 24-hour urinary microalbuminuria quantification the selected patients were started on losartan 50 mg/day for a six-month period. Monthly follow-ups were done to monitor the blood pressure, glycemic control, urea/creatinine/potassium levels and any untoward effects of losartan therapy. Quantitative microalbuminuria was repeated at the end of study. Out of the 171 patients, 149 (87.1%) had significant albuminuria reduction >30.0% of their baseline and the variable of final outcome of intervention (urinary albumin in mg/dl) was significantly reduced (Mean  $101.9 \pm SD 21.7$  baseline and  $47.5 \pm 12.9$  post therapy) with  $p < 0.001$  and with minimal side-effects. These anti-albuminuric effects of losartan were reversible as seen on rechecking the urinary albumin two months after discontinuation of treatment. Losartan was well tolerated and demonstrated significant anti-proteinuric effects in patients with T2DM with early nephropathy independent of hypertension, warranting further long-term large-scale studies to prove its usefulness as preventive therapy for diabetic nephropathy.

**Keywords:** Diabetes mellitus type 2, diabetic nephropathy, microalbuminuria, losartan, angiotensin receptor blocker.

## INTRODUCTION

Type-2 diabetes mellitus (T2DM) is a worldwide pandemic and WHO predicts that the current figure of 170 million affected patients with diabetes will more than double to 370 million patients by the year 2030.<sup>1</sup> Pakistan is currently sixth in the list of countries with highest number of estimated cases of diabetes mellitus.<sup>2</sup> Approximately one third of patients with T2DM will develop diabetic nephropathy, which is one of the leading cause of chronic renal failure.<sup>3</sup> Diabetic nephropathy (DN) is a clinical syndrome characterized by persistent albuminuria >300 mg/dl or 200 mcg/min along with relentless decline in GFR and elevated blood pressure. The first sign of renal involvement in diabetic nephropathy is microalbuminuria i.e. 24-hour urinary albumin of 30-300 mg/dl or urinary microalbumin excretion rate of 20-200 mcg/min, which can not be detected on routine methods of protein estimation. Gradually this progresses to proteinuria and overt nephropathy following which the GFR declines by 10-12 ml/min/year and hypertension ensues eventually leading to end stage renal disease (ESRD),<sup>4</sup> which has dismal survival rates even in the developed world.<sup>5</sup>

Microalbuminuria is an early indicator of diabetic nephropathy and associated with increased risk of progressiveness of renal disease in T2DM.<sup>6</sup> Apart from that it is also an independent risk factor for vascular diseases as 40.0-50.0% patients of T2DM with microalbuminuria die from cardiovascular diseases.<sup>7</sup> The prevalence of microalbuminuria is 38.9% in Asian T2DM patients Microalbuminuria prevalence study cohort,<sup>8</sup> and 34.0% in Karachi, Pakistan<sup>9</sup> as compared 17.0-21.0% in overall western population based studies.<sup>10</sup> It is recommended that screening for microalbuminuria be done on an annual basis in patients with T2DM for early identification and intervention.<sup>11</sup> Therapeutic measures that reduce albuminuria/proteinuria also retard the progression of renal disease as shown in trials with T2DM patients with overt nephropathy where reduction in proteinuria >30.0% below baseline value is associated with better preservation of renal function.<sup>12</sup> These measures include achieving a target blood pressure of less than 130/80 and use of various pharmacological

agents like Angiotensin receptor blockers (ARB), Angiotensin converting enzyme inhibitors (ACEI) and non-dihydropyridine Calcium channel blockers, which have shown to be successful in reducing albuminuria.<sup>13</sup> The anti-albuminuric effects appear to be at least partly independent of the blood pressure reduction caused by these agents,<sup>14-16</sup> although some studies have not confirmed this finding.<sup>17</sup> Since a prominent role in the pathogenesis of diabetic nephropathy is played by Angiotensin II via renin-angiotensin system, therefore both preventing the formation of angiotensin II by ACE inhibition and blockade of the angiotensin receptor may be considered as renoprotective. Recent trials have shown ARBs to be superior in reducing diabetic nephropathy as compared to ACEI by specifically inhibiting angiotensin II mediated efferent arteriolar vasoconstriction and reducing intraglomerular pressure with less bradykinin mediated side effects.<sup>18</sup> Apart from their antihypertensive properties some ARBs like losartan demonstrates anti-platelet activity,<sup>19</sup> as well as uricosuric properties.<sup>20</sup>

The trials of angiotensin-receptor antagonists in hypertensive patients with type 1 or 2 diabetes mellitus and microalbuminuria showed a reduction in albumin excretion, regardless of pretreatment levels.<sup>21-23</sup> In RENAAL (The Reduction of Endpoints in T2DM with the Angiotensin II Antagonist Losartan study) and IDNT (Irbesartan Diabetic Nephropathy Trial), losartan and irbesartan, respectively, reduced proteinuria and slowed the progression of diabetic nephropathy in hypertensive patients with type 2 diabetes.<sup>24,25</sup> Therefore, therapy that interferes with the renin-angiotensin-aldosterone system should probably be initiated when microalbuminuria develops in order to reduce albumin excretion and the associated risk for overt nephropathy.

The purpose of this study was to see whether losartan, a potent orally active and highly specific angiotensin II type 1 receptor blocker, could reduce microalbuminuria in normotensive patients with T2DM as almost all the previous international studies on this subject have investigated hypertensive patients and there have been no local studies on reduction of microalbuminuria.

## SUBJECTS AND METHODS

To assess the change in 24-hour urinary microalbuminuria in patients with Type-2 Diabetes mellitus without preexisting hypertension with the use of losartan daily over a six-month period without any major side-effects or complications.

**Study Design:** Interventional Phase Two Clinical Trial. Randomization was not possible due to our tertiary hospital catering for multitudes of population. The placebo-control group was abandoned because of objection of our hospital's ethical committee citing reason that knowingly giving microalbuminuric/proteinuric patients a placebo-drug (vitamin B complex) would actually give them no benefit and may actually put them at more risk. All patients gave written informed consent and guidelines of good clinical practice were followed.

**Place and duration of study:** This prospective study was done at Outpatient Diabetic Clinic of Jinnah Hospital Lahore for six months from May 28, 2006 to November 27, 2006 initially and we continued to follow these patient for another two months from November 27, 2006 to January 30<sup>th</sup> 2007.

**Patients:** One hundred eighty seven consecutive patients of Type 2 diabetes mellitus without hypertension were selected via non-probability purposive sampling after obtained an informed consent explaining them the risks and benefits of the study. The patients with established T2DM by ADA criteria,<sup>26</sup> for more than two years on either oral glycemics or diet controlled were included. Microalbuminuria was defined as a urinary albumin excretion rate of 20 to 200 mcg/min or 24-hour urinary albumin of 30-300 mg/dl. The current definition of normotension is a blood pressure less than 140/90 mm Hg, with a blood pressure lowering target of less than 130/80 mm Hg in hypertensive adults with diabetes mellitus. Hypertension was ruled out by history and examination. History regarding any past renal illness and drug history was taken and the patients had routine investigations esp. urinalysis to exclude patients with proteinuria or evidence of non-diabetic renal disease. Patients with history of hypersensitivity reactions to losartan, postural hypotension with systolic postural drop >20 mm of Hg, comorbid illnesses, pregnant ladies and poorly controlled diabetics (at least two episodes of symptomatic hypoglycemia or blood glucose levels >400 mg/dl on follow-up or baseline HbA<sub>1C</sub> >8) were excluded. We also excluded patients with a myocardial infarction or cerebrovascular events within the past one year, unstable angina pectoris, or symptomatic heart failure; patients with electrocardiographic abnormalities (atrioventricular conduction disturbances, sick sinus syndrome, atrial fibrillation, or other clinically significant rhythm disturbances), acute renal failure, chronic glomerulonephritis, polycystic kidney disease and patients with serum creatinine level greater than 1.5 mg/dL. After being screened for microalbuminuria by MICRAL test,<sup>27</sup> the patients testing positive were selected and an informed consent was obtained. The patients were advised against using ophthalmic preparations containing beta-blocking agents, steroids, lithium or any nephrotoxic drugs.

**Intervention and Measurements:** The patients who met all study criteria were selected and they underwent 24-hour urinary microalbuminuria quantification and were then put on losartan 50 mg/day for a six-month

period during which time patients were followed up monthly for monitoring of blood pressure, glycemic control and routine labs like urea/creatinine, urinalysis etc. The losartan treatment to the patients was provided free of cost via samples from hospital administration. Quantitative microalbuminuria was rechecked at three months and at end of six months. The losartan therapy was stopped at six months and quantitative microalbuminuria was repeated two months after stopping treatment. The data collected via proforma was analyzed by SPSS package for Microsoft Windows version 10.0. The variable of final outcome of intervention (losartan) was computed as Means and Standard deviations of baseline and after treatment. The numerical difference observed was tested for significance by applying the t-test.

## RESULTS

Out of the 187 patients, there 16 patients were lost in follow-up. There were 81 (47.4%) females and 90 (52.6%) males in our remaining 171 patients. We found that out of 171 patients, 149 (87.1%) had significant albuminuria reduction >30% of their baseline, 14 patients (8.2%) had mild reduction 10-30% and 8 patients (4.7%) had minimal or no change. The variable of final outcome of intervention (urinary albumin in mg/dl) with baseline of Mean  $101.9 \pm SD 21.7$ , and  $47.5 \pm 12.9$  after 6 months of losartan therapy, and the difference observed was found to be significant with  $p < 0.001$ . The changes in blood pressure were rather insignificant and did not correlate with the microalbuminuria reduction with baseline mean blood pressures being  $134.3 \pm SD 8.6$  systolic and  $82.3 \pm 11.4$  diastolic and during treatment at five months interval, the mean blood pressures were  $131.1 \pm 12.6$  systolic and  $78.6 \pm 13.4$  diastolic.

After stopping losartan and finishing of hospital's supply at the end of six months interval, we continued to follow these patients for another two months and observed 141 patients stopped using losartan while 21 patients were either using losartan regularly or on and off via self-purchase. We had advised all the patients regarding the usefulness of the drug, giving them the choice to purchase. 9 patients were lost in follow-up. We repeated quantitative microalbuminuria in these 141 (76 males and 65 female) patients, two months after stopping losartan and found that 119 (84.0%) patients had again achieved microalbuminuria levels nearly equivalent to their baseline with minimal or no change. The final urinary albumin levels in these patients were Mean  $91.8 \pm SD 17.3$  (mg/dl) two months after stopping losartan, which showed that the anti-albuminuric effects of losartan were reversible after discontinuation of treatment and this effect was disproportionate to the changes in blood pressure.

Regarding the side-effects of losartan therapy, only 15 patients reported mild dizziness during the first week of treatment which resolved on its own but 3 of these patients continued to report postural lightheadedness with postural drop greater than 10 mm of Hg. The losartan tablet of 50 mg was divided in two equal doses of 25 mg each, given 12 hours apart in these three patients and all of them reported improvement in symptoms with reduction of postural drop to within normal limits within two weeks. In all these patients the creatinine, urea, potassium levels all remained within normal range without any significant change (Table 2).

**Limitations:** Our study was a single centered, non-randomized study due to lack of resources and the setup of our tertiary care hospital. , and our sample size and duration of study was probably not enough to make very significant recommendations.

## DISCUSSION

Diabetic nephropathy (DN) is the single largest cause of end-stage renal disease (ESRD) in USA and Europe accounting for ~40.0% and 20% new cases respectively,<sup>28</sup> and carries a terrible individual and societal burden. It is now regarded as a global pandemic with one-third ESRD cases world over being a sequelae of DN, of which microalbuminuria is a hallmark.<sup>29</sup> Studies have shown that microalbuminuria is a target to improve cardiovascular and renal outcomes, not only in diabetics but also in non-diabetics.<sup>30,31</sup>

Major clinical trials such as REENAL study has shown to effectively limit the progression of DN to ESRD by 18% while using losartan with 35% decrease in proteinuria as compared to placebo.<sup>32</sup> Another study, ELITE trial has shown losartan to be better tolerable in elderly with reduction in mortality.<sup>33</sup> In MARVAL study, blockage of rennin-angiotensin by Valsartan has shown beneficial effects in the form of decreased urinary albumin excretion.<sup>34</sup> Studies have shown that ACEI reduces albumin excretion in normotensive patients with type 1 or type 2 diabetes,<sup>35,36</sup> but anti-proteinuric effects of ARBs in normotensive diabetic patients have not been fully established.

A randomized clinical trial in Netherlands has earlier shown losartan to be effective in microalbuminuria reduction in normotensive T2DM patients over a 10-week period, which was independent of associated reduction in blood pressure.<sup>37</sup> Therefore, therapy that interferes with the renin-angiotensin-aldosterone system

should be initiated when microalbuminuria develops to reduce albumin excretion and diabetic nephropathy. A possible site of action of angiotensin-receptor antagonists in normotensive diabetic patients is the vascular endothelium. Endothelial dysfunction has been associated with increased urinary albumin excretion, as well as with an increased risk for cardiovascular events in type 2 diabetes.<sup>38</sup> Urinary albumin excretion reduction may reflect recovery of endothelial function and may predict a reduction in the risk for complications.

Most previous studies on this subject have investigated hypertensive patients and so our study emphasized on the use of losartan to prevent early diabetic nephropathy unrelated to hypertension, so that development, progression and other long term complications of DN can be halted.

Losartan, an ARB, demonstrated significant anti-albuminuric ability in normotensive patients with T2DM with early nephropathy, which favors its use in treating T2DM patients with nephropathy independent of hypertension. Losartan was well tolerated in our study and it shows that normotensive patients can be treated safely with it. Since there are many factors that contribute to diabetic kidney damage, of which microalbuminuria is an indicator, the treatment should also target multiple factors including strict blood glucose and blood pressure control and using agents like losartan which inhibits the rennin-angiotensin system.

We recommend that further large-scale long-term prospective placebo-controlled clinical trials should be done in normotensive diabetic patients using ARBs to obtain more evidence, so that in future early start of these drugs in T2DM patients with normal blood pressures can be advocated in order to prevent morbidity and mortality associated with diabetic nephropathy.

### FUNDING SOURCE

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### REFERENCES

1. World Health Organisation. The Diabetes Program 2004. Available at:<http://www.who.int/diabetes/en/>. September 21, 2004.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27: 1047-53.
3. Remuzzi G, Schieppati A, Ruggenenti P. Clinical Practice. Nephropathy in patients with type 2 diabetes. *New Engl J Med* 2002; 346: 1145-51.
4. Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *New Engl J Med* 2001; 345: 870-8.
5. Ritz E, Rychlik I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes – a medical catastrophe of worldwide dimensions. *Amer J Kidney Dis* 1999; 34: 795-808.
6. Ghafoor F, Bano KA, Malik T, Mahmood S, Amanullah Khan. Microalbuminuria as an indicator of kidney function among diabetics. *J Coll Physicians Surg Pak* 2004; 14: 670-2.
7. Ritz E. Albuminuria and vascular damage – the vicious twins. *New Engl J Med* 2003; 348: 2349-52.
8. Wu AY, Kong NC, de Leon FA *et al*. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. *Diabetologia* 2005; 48: 17-26.
9. Ahmedani MY, Hydrie MZ, Iqbal A, Gul A, Mirza WB, Abdul Basit. Prevalence of microalbuminuria in type 2 diabetic patients in Karachi: Pakistan: a multi-center study. *J Pak Med Assoc* 2005; 55: 382-6.
10. Parving HH, Osterby R, Ritz E. Diabetic nephropathy. In: Brenner BM, editor. *The kidney*. Philadelphia: Saunders 2000: 1731-73.
11. American Diabetes Association. Diabetic nephropathy. Position Statement. *Diabetes Care* 2002; 25: 85-9.
12. Onuigbo M, Weir MR. Evidence-based treatment of hypertension in patients with diabetes mellitus. *Diabetes* 2003; 5: 13-26.
13. Ruggenenti P, Fassi A, Ilieva AP *et al*. Bergamo Nephrologic Diabetes Complications Trial (BENEDICT) Investigations. Preventing microalbuminuria in type 2 diabetes. *New Engl J Med* 2004;351:1941-51
14. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. *Lancet* 2000; 355: 253-9.
15. Mathiesen ER, Hommel E, Hansen HP, Smidt UM, Parving HH. Randomised controlled trial of long term efficacy of captopril on preservation of kidney function in normotensive patients with insulin dependent diabetes and microalbuminuria. *Brit Med J* 1999; 319: 24-5.
16. Ahmad J, Siddiqui MA, Ahmad H. Effective postponement of diabetic nephropathy with enalapril in normotensive type 2 diabetic patients with microalbuminuria. *Diabetes Care* 1997; 20: 1576-81.
17. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. *Brit Med J* 1998; 317: 713-20.
18. Parvanova A, Chiurciu C, Ruggenenti P, Remuzzi G. Inhibition of the renin-angiotensin system and cardio-renal protection: focus on losartan and angiotensin receptor blockade. *Expert Opin Pharmacother* 2005; 6: 1931-42

19. Nunez A, Gomez J, Zalba LR, *et al.* Losartan inhibits in vitro platelet activation: comparison with candesartan and valsartan. *J Renin Angiotensin Aldosterone Syst* 2000; 1: 175-9.
20. Sica DA, Schoolwerth AC. Part 1. Uric acid and losartan. *Curr Opin Nephrol Hypertens* 2002; 11: 475-82.
21. Andersen S, Tarnow L, Rossing P, Hansen BV, Parving HH. Renoprotective effects of angiotensin II receptor blockade in type 1 diabetic patients with diabetic nephropathy. *Kidney Int'l* 2000; 57: 601-6.
22. Lacourcière Y, Bé langer A, Godin C, Halle´ JP, Ross S, Wright N, *et al.* Long-term comparison of losartan and enalapril on kidney function in hypertensive type 2 diabetics with early nephropathy. *Kidney Int'l* 2000; 58: 762-9.
23. Lozano JV, Llisterri JL, Aznar J, Redon J. Losartan reduces microalbuminuria in hypertensive microalbuminuric type 2 diabetics. *Nephrol Dial Transplant* 2001; 16 Suppl 1: 85-9.
24. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, *et al.* Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *New Engl J Med* 2001; 345: 851-60.
25. Brenner BM, Cooper ME, de Zeeuw D *et al.* Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *New Engl J Med* 2001; 345: 861-9.
26. American Diabetes Association. Report of the expert committee on diagnosis and classification of Diabetes Mellitus. *Diabet Care* 1997; 7: 1183-97.
27. Spooren PF, Lekkerkerker JF, Vermes I. Micral-test: a qualitative dipstick test for micro-albuminuria. *Diabetes Res Clin Pract* 1992. 18: 83–87.
28. National Institutes of Health: Excerpts from United States Renal Data System's 2000 annual data report: atlas of end-stage renal disease in the United States: economic costs of ESRD. *Amer J Kidney Dis* 2000; 36: 163-76.
29. Rossing P. Diabetic nephropathy: worldwide epidemic and effects of current treatment on natural history. *Curr Diab Rep* 2006; 6: 479-83.
30. Basi S, Lewis JB. Microalbuminuria as a target to improve cardiovascular and renal outcomes. *Amer J Kidney Dis* 2006; 47: 927-46.
31. Jensen JS. Microalbuminuria is a strong determinant for ischemic heart disease—also among non-diabetics. *Ugeskr Laeger* 2007; 169: 485-7.
32. Hostetter TH. Prevention of end-stage renal disease due to type 2 diabetes. *New Engl J Med* 2001; 345: 910-2.
33. Cowley AJ, Wiens BL, Segal R, Rich MW, Santanello NC, Dasbach EJ, Pitt B; ELITE Investigators. Evaluation of Losartan in the Elderly. Randomised comparison of losartan vs. captopril on quality of life in elderly patients with symptomatic heart failure: the losartan heart failure ELITE quality of life substudy. *Qual Life Res* 2000; 9: 377-84.
34. Viberti G, Wheeldon NM. Microalbuminuria reduction with valsartan in patients with type 2 diabetes mellitus: a blood pressure independent effect. *Circulation* 2002; 106: 672-8
35. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. The EUCLID Study Group. *Lancet* 1997; 349: 1787-92.
36. Ravid M, Brosh D, Levi Z, Bar-Dayyan Y, Ravid D, Rachmani R. Use of enalapril to attenuate decline in renal function in normotensive, normoalbuminuric patients with type 2 diabetes mellitus. A randomized, controlled trial. *Ann Intern Med* 1998; 128: 982-8.
37. Zandbergen AA, Baggen MG, Lamberts SW, Bootsma AH, de Zeeuw D, Ouwendijk RJ. Effect of losartan on microalbuminuria in normotensive patients with type 2 diabetes mellitus. A randomized clinical trial. *Ann Intern Med* 2003; 139: 90-6.
38. Stehouwer CD, Nauta JJ, Zeldenrust GC, Hackeng WH, Donker AJ, den Ottolander GJ. Urinary albumin excretion, cardiovascular disease, and endothelial dysfunction in non-insulin-dependent diabetes mellitus. *Lancet* 1992; 340: 319-23.

**Table-1:** Baseline characteristics of patients under study before starting losartan

<b>Characteristics</b>	<b>Mean <math>\pm</math> SD (n=171)</b>
Age (years)	53.7 $\pm$ 11.1
Weight (kg)	92.3 $\pm$ 21.1
Height (m)	1.45 $\pm$ 0.29
BMI (kg/m <sup>2</sup> )	32.3 $\pm$ 10.4
Systolic blood pressure (mm of Hg)	134.3 $\pm$ 8.6
Diastolic blood pressure (mm of Hg)	82.3 $\pm$ 11.4
Serum creatinine (mg/dl)	1.2 $\pm$ 0.3
Random blood sugars levels (mg/dl)	182.9 $\pm$ 81.4
Fasting blood sugars levels (mg/dl)	122.5 $\pm$ 41.7
Glycosylated hemoglobin (%)	7.2 $\pm$ 1.0
24-hour urinary microalbumin levels (mg/dl)	101.9 $\pm$ 21.7

**Table-2:** Characteristics before starting losartan, after 6-months losartan and two months after stopping therapy

<b>Laboratory/ Physical examination Characteristics</b>	<b>Before starting losartan therapy  Mean <math>\pm</math> SD  (n=171)</b>	<b>After 6 months losartan therapy  Mean <math>\pm</math> SD  (n=171)</b>	<b>2 months after stopping losartan  Mean <math>\pm</math> SD  (n=171)</b>
Systolic blood pressure (mm of Hg)	134.3 $\pm$ 8.6	131.1 $\pm$ 12.6	132.6 $\pm$ 10.9
Diastolic blood pressure (mm of Hg)	82.3 $\pm$ 11.4	78.6 $\pm$ 13.4	79.7 $\pm$ 10.3
Serum creatinine (mg/dl)	1.2 $\pm$ 0.3	1.3 $\pm$ 0.4	1.3 $\pm$ 0.3
Random blood sugars levels (mg/dl)	182.9 $\pm$ 81.4	161.3 $\pm$ 51.2	173.1 $\pm$ 63.8
Fasting blood sugars levels (mg/dl)	122.5 $\pm$ 41.7	112.5 $\pm$ 26.5	115.8 $\pm$ 31.1
Serum Potassium (mEq/L)	4.3 $\pm$ 0.8	4.4 $\pm$ 1.1	4.2 $\pm$ 0.9
24-hour urinary microalbumin (mg/dl)	101.9 $\pm$ 21.7	47.5 $\pm$ 12.9	91.8 $\pm$ 17.3